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January 4, 2005

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Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

**Mail Stop: Amendment**

Re: U.S. Utility Patent Application  
Appl. No. 10/821,128; Filed: April 9, 2004  
For: **Methods of Synthesizing and Labeling Nucleic Acid Molecules**  
Inventors: LEE *et al.*  
Our Ref: 0942.5690001/RWE/JKM

Sir:

Transmitted herewith for appropriate action are the following documents:

1. Information Disclosure Statement Under 37 C.F.R. § 1.97(b);
2. List of cited references on Form PTO-1449 (14 sheets); and
3. Copies of references **AL1-AP1, AR1-AT1, AL2-AP2, AR2-AT2, AL3-AP3 and AR3-AT14** listed on Form PTO-1449 (57 documents); and
4. One (1) return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

Commissioner for Patents  
January 4, 2005  
Page 2

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Robert W. Esmond  
Attorney for Applicants  
Registration No. 32,893

RWE/JKM:bac  
Enclosures

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Lee *et al.*

Appl. No.: 10/821,128

Filed: April 9, 2004

For: **Methods of Synthesizing and  
Labeling Nucleic Acid Molecules**

Confirmation No.: 8246

Art Unit: 1653

Examiner: *To Be Assigned*

Atty. Docket: 0942.5690001/RWE/JKM

**Information Disclosure Statement Under 37 C.F.R. § 1.97(b)**

Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. In accordance with 37 C.F.R. § 1.98(a)(2), copies of U.S. patents and patent application publications cited on the attached Form PTO-1449 are not submitted. Copies of documents AL1 to AP3 and AR1 to AT14 are provided.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached Form PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may

not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith.

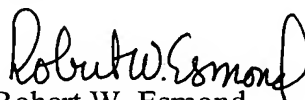
This Information Disclosure Statement is being filed within before the mailing of a first Office Action on the merits. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Robert W. Esmond  
Attorney for Applicants  
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Date: Jan. 4, 2005

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FORM PTO-1449

JAN 04 2005

## INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.  
0942.5690001/RWE/J-MAPPLICATION NO.  
10/821,128FIRST NAMED INVENTOR  
Lee *et al.*FILING DATE  
April 9, 2004ART UNIT  
1653

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA1	4,038,480	07/26/1977	Robins <i>et al.</i>			09/17/1973
	AB1	4,088,639	05/09/1978	Zappelli <i>et al.</i>			06/12/1975
	AC1	4,213,893	07/22/1980	Carrico <i>et al.</i>			10/12/1978
	AD1	4,255,566	03/10/1981	Carrico <i>et al.</i>			02/19/1980
	AE1	4,443,594	04/17/1984	Bückmann			09/08/1981
	AF1	4,460,772	07/17/1984	Benovic <i>et al.</i>			05/11/1983
	AG1	4,582,789	04/15/1986	Sheldon, III <i>et al.</i>			12/18/1984
	AH1	4,599,303	07/08/1986	Yabusaki <i>et al.</i>			12/12/1983
	AI1	4,617,261	10/14/1986	Sheldon, III <i>et al.</i>			10/25/1985
	AJ1	4,683,195	07/28/1987	Mullis <i>et al.</i>			02/07/1986
	AK1	4,683,202	07/28/1987	Mullis			10/25/1985

## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL1	WO 92/06188 A2	04/16/1992	WIPO			Yes No
	AM1	WO 92/06200 A1	04/16/1992	WIPO			Yes No
	AN1	EP 0 329 822 B1	06/08/1994	Europe			Yes No
	AO1	WO 95/35505 A1	12/28/1995	WIPO			Yes No
	AP1	WO 96/10640 A1	04/11/1996	WIPO			Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	1	Agrawal, S., "Functionalization of Oligonucleotides with Amino Groups and Attachment of Amino Specific Reporter Groups," in: <i>Methods in Molecular Biology, Vol. 26, Protocols for Oligonucleotide Conjugates</i> , Agrawal, S., ed., Humana Press, Totowa, NJ, pp. 93-120 (1994)
AS	1	Augustyns, K., <i>et al.</i> , "Synthesis of oligonucleotides modified in the sugar moiety," <i>Nucl. Acids Res. Symp. Series</i> 24:224, Oxford University Press (1991)
AT	1	Baird, G.S., <i>et al.</i> , "Biochemistry, mutagenesis, and oligomerization of DsRed, a red fluorescent protein from coral," <i>Proc. Natl. Acad. Sci. USA</i> 97:11984-11989, National Academy of Sciences (2000)

EXAMINER

DATE CONSIDERED

**EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449  INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 0942.5690001/RWE/J-M	APPLICATION NO. 10/821,128
	FIRST NAMED INVENTOR Lee <i>et al.</i>	
	FILING DATE April 9, 2004	ART UNIT 1653

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA2	4,707,440	11/17/1987	Stavrianopoulos			01/30/1984
	AB2	4,711,955	12/08/1987	Ward <i>et al.</i>			05/23/1983
	AC2	4,737,454	04/12/1988	Dattagupta <i>et al.</i>			05/18/1984
	AD2	4,743,535	05/10/1988	Carrico			11/07/1984
	AE2	4,770,992	09/13/1988	Van den Engh <i>et al.</i>			11/27/1985
	AF2	4,828,979	05/09/1989	Klevan <i>et al.</i>			11/08/1984
	AG2	4,889,818	12/26/1989	Gelfand <i>et al.</i>			06/17/1987
	AH2	4,965,188	10/23/1990	Mullis <i>et al.</i>			06/17/1987
	AI2	5,244,797	09/14/1993	Kotewicz <i>et al.</i>			03/18/1991
	AJ2	5,374,553	12/20/1994	Gelfand <i>et al.</i>			08/13/1990
	AK2	5,409,818	04/25/1995	Davey <i>et al.</i>			06/24/1988

## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL2	WO 98/06736 A1	02/19/1998	WIPO			Yes No
	AM2	WO 98/08981 A1	03/05/1998	WIPO			Yes No
	AN2	WO 98/47912 A1	10/29/1998	WIPO			Yes No
	AO2	WO 98/51699 A1	11/19/1998	WIPO			Yes No
	AP2	WO 99/15702 A1	04/01/1999	WIPO			Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	2	Barnes, W.M., "The fidelity of <i>Taq</i> polymerase catalyzing PCR is improved by an N-terminal deletion," <i>Gene</i> 112:29-35, Elsevier Science Publishers B.V. (1992)
	AS	2	Barrio, J.R., <i>et al.</i> , "Fluorescent Adenosine and Cytidine Derivatives," <i>Biochem. Biophys. Res. Commun.</i> 46:597-604, Academic Press, Inc. (1972)
	AT	2	Bevis, B.J. and Glick, B.S., "Rapidly maturing variants of the <i>Discosoma</i> red fluorescent protein (DsRed)," <i>Nature Biotechnol.</i> 20:83-87, Nature Publishing Group (January 2002)

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	FIRST NAMED INVENTOR Lee <i>et al.</i>	
	FILING DATE April 9, 2004	ART UNIT 1653

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA3	5,436,149	07/25/1995	Barnes			02/19/1993
	AB3	5,455,166	10/03/1995	Walker			01/09/1992
	AC3	5,512,462	04/30/1996	Cheng			02/25/1994
	AD3	5,668,005	09/16/1997	Kotewicz <i>et al.</i>			03/12/1996
	AE3	5,948,614	09/07/1999	Chatterjee			09/06/1996
	AF3	6,015,668	01/18/2000	Hughes <i>et al.</i>			09/06/1996
	AG3	6,063,608	05/16/2000	Kotewicz <i>et al.</i>			02/10/1997
	AH3	2001/0041334 A1	11/15/2001	Rashtchian <i>et al.</i>			12/21/2000
	AI3	2002/0012970 A1	01/31/2002	Smith <i>et al.</i>			03/30/2001
	AJ3	2002/0090618 A1	07/11/2002	Smith <i>et al.</i>			05/01/2001
	AK3	2003/0003452 A1	01/02/2003	Potter <i>et al.</i>			03/15/2001

## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL3	WO 00/52191 A1	09/08/2000	WIPO			Yes No
	AM3	WO 01/092500 A1	12/06/2001	WIPO			Yes No
	AN3	WO 01/68895 A1	09/20/2001	WIPO			Yes No
	AO3	WO 02/04022 A1	01/17/2002	WIPO			Yes No
	AP3	EP 0 684 315 B1	06/26/2002	WIPO			Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	3	Campbell, R.E., <i>et al.</i> , "A monomeric red fluorescent protein," <i>Proc. Natl. Acad. Sci. USA</i> 99:7877-7882, National Academy of Sciences (June 2002)
	AS	3	Chiesa, A., <i>et al.</i> , "Recombinant aequorin and green fluorescent protein as valuable tools in the study of cell signalling," <i>Biochem. J.</i> 355:1-12, The Biochemical Society (2001)
	AT	3	Churchich, J.E., "Fluorescence studies on soluble ribonucleic acid labelled with acriflavine," <i>Biochim. Biophys. Acta</i> 75:274-276, Elsevier Publishing Company (1963)

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	AA						
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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	4	Cristofari, G., <i>et al.</i> , "Characterization of Active Reverse Transcriptase and Nucleoprotein Complexes of the Yeast Retrotransposon Ty3 <i>in Vitro</i> ," <i>J. Biol. Chem.</i> 274:36643-36648, American Society for Biochemistry and Molecular Biology, Inc. (1999)
	AS	4	Draper, D.E. and Gold, L., "A Method for Linking Fluorescent Labels to Polynucleotides: Application to Studies of Ribosome-Ribonucleic Acid Interactions," <i>Biochem.</i> 19:1774-1781, American Chemical Society (1980)
	AT	4	Folsom, V., <i>et al.</i> , "Detection of DNA Targets with Biotinylated and Fluoresceinated RNA Probes," <i>Anal. Biochem.</i> 182:309-314, Academic Press, Inc. (1989)

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	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>5</u>	Flaman, J.-M., <i>et al.</i> , "A rapid PCR fidelity assay," <i>Nucl. Acids Res.</i> 22:3259-3260, Oxford University Press (1994)
	AS	<u>5</u>	Gebeyehu, G., <i>et al.</i> , "Novel biotinylated nucleotide - analogs for labelling and colorimetric detection of DNA," <i>Nucl. Acids Res.</i> 15:4513-4534, IRL Press Ltd. (1987)
	AT	<u>5</u>	Gerard, G.F., <i>et al.</i> , "cDNA Synthesis by Moloney Murine Leukemia Virus RNase H-Minus Reverse Transcriptase Possessing Full DNA Polymerase Activity," <i>Focus</i> 14:91-93, Life Technologies, Inc. (1992)

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	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	6	Goodchild, J., "Conjugates of Oligonucleotides and Modified Oligonucleotides: A Review of Their Synthesis and Properties," <i>Bioconj. Chem.</i> 1:165-187, American Chemical Society (1990)
	AS	6	Gubler, U. and Hoffman, B.J., "A simple and very efficient method for generating cDNA libraries," <i>Gene</i> 25:263-269, Elsevier Science Publishers (1983)
	AT	6	Guzaev, A., <i>et al.</i> , "Synthesis and Primer Properties of Oligonucleotides Containing 3'-Deoxypsicothymidine Units, Labeled with Fluorescein at the 1'-Position," <i>Bioconj. Chem.</i> 5:501-503, American Chemical Society (1994)

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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>I</u>	Hileman, R.E., <i>et al.</i> , "Synthesis and Characterization of Conjugates Formed between Periodate-Oxidized Ribonucleotides and Amine-Containing Fluorophores," <i>Bioconj. Chem.</i> 5:436-444, American Chemical Society (1994)
	AS	<u>I</u>	Knop, M., <i>et al.</i> , "Improved Version of the Red Fluorescent Protein (drFP583/DsRed/RFP)," <i>BioTechniq.</i> 33:592-602, Eaton Publishing Co. (July 2002)
	AT	<u>I</u>	Kotewicz, M.L., <i>et al.</i> , "Isolation of cloned Moloney murine leukemia virus reverse transcriptase lacking ribonuclease H activity," <i>Nucl. Acids Res.</i> 16:265-277, IRL Press Ltd. (1988)

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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	8	Krug, M.S. and Berger, S.L., "First-Strand cDNA Synthesis Primed with Oligo(dT)," <i>Meth. Enzymol.</i> 152:316-325, Academic Press, Inc. (1987)
	AS	8	Larrick, J.W., <i>et al.</i> , "Green fluorescent protein: untapped potential in immunotechnology," <i>Immunotechnol.</i> 1:83-86, Elsevier Science B.V. (1995)
	AT	8	Lawyer, F.C., <i>et al.</i> , "High-level Expression, Purification, and Enzymatic Characterization of Full-length <i>Thermus aquaticus</i> DNA Polymerase and a Truncated Form Deficient in 5' to 3' Exonuclease Activity," <i>PCR Meth. Appl.</i> 2:275-287, Cold Spring Harbor Laboratory Press (1993)

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	AM						Yes No
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	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	<u>9</u>	Leonard, N.J. and Tolman, G.L., "Fluorescent Nucleosides and Nucleotides," in: <i>Chemistry, Biology, and Clinical Uses of Nucleoside Analogs</i> , Bloch, A., ed., The New York Academy of Sciences, New York, NY, pp.43-58 (1975)
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AT	<u>9</u>	Maniatis, T., <i>et al.</i> , "The Isolation of Structural Genes from Libraries of Eucaryotic DNA," <i>Cell</i> 15:687-701, MIT (1978)

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FORM PTO-1449

INFORMATION DISCLOSURE STATEMENTATTY. DOCKET NO.  
0942.5690001/RWE/J-MAPPLICATION NO.  
10/821,128FIRST NAMED INVENTOR  
Lee *et al.*FILING DATE  
April 9, 2004ART UNIT  
1653**U.S. PATENT DOCUMENTS**

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	AL						Yes No
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	AN						Yes No
	AO						Yes No
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	AR	<u>11</u>	Okayama, H. and Berg, P., "High-Efficiency Cloning of Full-Length cDNA," <i>Molec. Cell. Biol.</i> 2:161-170, American Society for Microbiology (1982)
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	AR	<u>12</u>	Sacchetti, A., <i>et al.</i> , "The molecular determinants of the efficiency of green fluorescent protein mutants," <i>Histol. Histopathol.</i> 15:101-107, Jiménez Godoy, S.A. (2000)
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	AR	<u>13</u>	Terskikh, A.V., <i>et al.</i> , "Analysis of DsRed Mutants," <i>J. Biol. Chem.</i> 277:7633-7636, American Society for Biochemistry and Molecular Biology, Inc. (March 2002)
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